UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,931	12/27/2001	Vera Mahler	0273-0007	7190

7590 06/20/2006

Toni-Junell Herbert
Reed Smith LLP
3110 Fairview Park Drive
Suite 1400
Falls Church, VA 22042

EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/026,931	MAHLER ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-34,37-41 and 43-52* is/are pending in the application.

4a) Of the above claim(s) *24-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 34, 37-41 and 43-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Please note that the examiner of record for your application has changed. To aid in paper matching, please address all future correspondence to Michael Szperka, Art Unit 1644, Technology Center 1600.

Applicant's response and amendments received March 28, 2006 are acknowledged.

Claims 1-23, 35, 36, and 42 have been canceled.
Claims 33, 37, and 47 have been amended.
Claims 49-52 have been added.
Claims 24-34, 37-41, and 43-52 are pending.
Claims 24-32 stand withdrawn from consideration as being drawn to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03, for reasons of record set forth in the Office Action mailed May 20, 2005.

Claims 33, 34, 37-41, 43-52 are under examination in this office action as they read on methods of treating IgE-mediated allergic disorders by administering allergen derivatives.

Claim Rejections - 35 USC § 102

2. The rejection of claims 33-34, 37-40 and 43-48 under 35 U.S.C. 102(e) as being anticipated by Ipsen et al., US Patent Application Publication 2004/0091500 A1, of record, for the reasons set forth in the Office Actions mailed 10/4/04 and 10/7/05, has been withdrawn in light of applicants amendments to the claims received March 28, 2006. Specifically, the claims now recite that administered allergen derivative induces IgE-blocking antibodies and comprises an IgE binding capacity of 50% or less as compared to the naturally occurring allergen. The methods taught by Ipsen et al. do not comprise both of these limitations and as such the rejection has been withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claim 37 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement due to the recitation "elimination of IgE binding" has been obviated by applicant's amendment of the claim received March 28, 2006 to recite "substantially no allergenic activity", support for which can be found on page 4 of the specification.

The following are new grounds of rejection.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 33, 34, 37-41, and 43-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 33 has been amended to recite that the administered derivatives are from naturally occurring grass pollen allergens, dependent claim 47 has been amended to recite that the grass pollen allergen is to be selected from the group consisting of alder, hazel, and birch, and dependent claims 46, 51 and 52 recite the specific birch allergen Bet v 1. Applicant's claims have thus defined alder, hazel, and birch, three kinds of trees, as being grasses. Tree pollen allergens and grass pollen allergens are recognized in the art as being structurally distinct from one another, as evidenced by chapters 10 and 11 of Lockey et al. (Allergens and Allergen Immunotherapy, third edition, 2004, pages 165-205, see entire document), and as such

the metes and bounds of claims 46, 47, 51 and 52 are unclear because trees are not grasses. Given that applicant has defined trees as members of the genus of grasses via the above indicated dependent claims, the metes and bound of the independent claim and the other dependent claims are also unclear because it is not known what other allergens applicant has encompassed by the recitation of grass pollen allergens in the independent claim. This is because applicant is using the term "grass pollen allergens" in a manner that is not consistent with the art as evidenced by Lockey et al., and additional guidance in the specification concerning the metes and bounds of the term "grass pollen allergens" cannot be located.

7. Claims 33, 34, 37-41, and 43-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Independent claim 33 recites that the administered allergen derivative induces IgE-blocking antibodies and that specific IgE binding to the administered derivative is 50% or less as compared with IgE binding to the naturally occurring allergen. The specification teaches on page 4 that the administered allergen derivative is to have less than 50% of the allergenic activity of the wildtype allergen from which it is derived, and defines allergenic activity as the capacity to induce an IgE response upon administration to a test animal. The specification further teaches on page 4 that the basophil histamine release assay is a preferred *in vitro* test for determining allergenic activity. The specification does not appear to support the limitation that specific IgE binding to the allergen derivative is 50% or less as compared to the wildtype allergen since the binding to preexisting IgE antibodies and the ability to elicit new IgE antibody production are distinct properties. For example, Valenta et al. teach an allergen derivative that binds preexisting IgE comparable to the wildtype allergen yet does not induce histamine release from basophils (WO 99/16467, see entire document, particularly lines 22-23 of

page 10, the paragraph spanning pages 11 and 12, and page 13). Note that all other claims under examination depend directly or indirectly from claim 33, and that none of these claims further limit the claimed invention such that the new matter is excluded.

Dependent claim 47 recites that grass pollen allergens are to be selected from the group consisting of alder, hazel, and birch, while dependent claims 46, 51 and 52 limit the grass pollen allergen to Bet v 1, the major allergen found in birch pollen. Tree pollen allergens and grass pollen allergens are generally recognized in the art as being structurally distinct from one another, as evidenced by chapters 10 and 11 of Lockey et al. (Allergens and Allergen Immunotherapy, third edition, 2004, pages 165-205, see entire document), and patients known to suffer from grass pollen allergies do not have antibodies that also bind the birch pollen allergen Bet v 1 as taught by Valenta et al. (ibid, see particularly the paragraph spanning pages 17 and 18). Further, the paragraph spanning pages 2 and 3 of the specification teaches that derivatives of allergenic proteins can be made from a non-limiting list of allergens that includes Bet v 1 and grass pollen allergens, but this paragraph does not teach that Bet v 1 is a grass pollen allergen. As such applicant's definition of alder, hazel, birch, and the specific allergen Bet v 1 as members of the genus of grass pollen allergens via the claims is new matter.

8. Claims 33, 34, 37-41, and 43-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating IgE-mediated birch pollen allergies by administering derivatives of the allergen Bet v 1, wherein the derivatives of Bet v 1 are selected from the group consisting of trimers of Bet v 1, the polypeptide consisting of amino acids 1-73 of Bet v1 and the polypeptide consisting of amino acids 74-159 of Bet v 1, and wherein said derivatives induce IgE-blocking antibodies and comprise reduced allergenic activity as compared to wildtype Bet v 1, does not reasonably provide enablement for a method of treating or preventing all IgE-mediated disorders by administering derivatives of grass pollen allergens wherein the derivatives induce IgE-blocking antibodies and comprise a specific IgE binding capacity that is 50% or less as compared to the naturally occurring allergen. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has claimed a method of treating or preventing IgE-mediated allergic disorders by repeatedly administering derivatives of a known allergen. The specification teaches many IgE-mediated disorders on page 1, and teaches that the IgE antibodies that are responsible for mediating these conditions are allergen specific. The claim recites that the administered agent is a modified grass pollen allergen, yet the claim preamble does not limit the IgE-mediated disorders to those that involve only grass-pollen allergen specific IgE antibodies. As such, it does not appear that applicant's method would treat or prevent all IgE-mediated allergic disorders since the IgE antibodies responsible for such disorders are often specific for allergens other than grass pollen, such as insect proteins and drugs (Ipsen et al. of record, see entire document, particularly paragraph 3).

Further, while the specification teaches methods for the treatment or prevention of allergic disorders (see particularly page 2 of the specification), the specification does not appear to define the term prevent. Allergic reactions occur subsequent to allergen reexposure, and as such therapy needs to be initiated prior to the development of an allergen specific IgE response to prevent the occurrence of an IgE mediated disorder. The development of an allergen specific IgE response is due to the complex interplay of environmental and genetic factors, and therefore it is not predictable who will or will not develop an allergic response to a given allergen (chapter 2 of Lockey et al. in Allergens and Allergen Immunotherapy, third edition, 2004, pages 37-50, see entire document particularly pages 42-46, Figure 2, and the salient points section spanning pages 47 and 48). The claims recite that the allergen derivative is to be administered to a patient in need thereof, but as discussed above it is unpredictable who will or will not develop an IgE-mediated disorder specific for a given allergen. As such the only identifiable patients in need of treatment are those already known to suffer from allergies specific for a given allergen. These patients currently have an ongoing IgE-mediated immune response directed to the specific allergen, and as such the IgE-mediated reaction cannot be prevented because it has already occurred.

Applicant's claimed method is also broad in that the independent claim recites a method wherein an agent is administered to a patient, wherein the agent is known to comprise the functional properties of inducing an IgE-blocking antibody response and having reduced specific IgE binding as compared to the naturally occurring allergen due to its selection via a recited screening protocol. The administered agent is a derivative of a naturally occurring allergen, and in the paragraph spanning pages 2 and 3, the specification teaches that derivatives of an allergen can be fragments, oligomers, and chemically modified forms of naturally occurring allergens as well as molecules obtained by site directed mutagenesis of an allergen protein.

Polypeptide derivatives of allergens are known in the art, and applicant has provided examples of three derivatives of Bet v 1, namely a trimer of Bet v 1, the polypeptide consisting of amino acids 1-73 of Bet v 1, and the polypeptide consisting of amino acids 74-159 of Bet v 1 to support the claimed invention. Claim 52 limits the invention in that the derivative used for immunotherapy is a trimer of Bet v 1, and this claim depends from claim 33, which recites the limitation that specific IgE binding to the derivative is 50% or less compared to the IgE binding to the naturally occurring allergen. Applicant discloses that the trimer of Bet v 1 was made as described in the prior art, and the indicated prior art document discloses that the trimer does not demonstrate a reduction in its specific IgE binding capacity (of record as reference L on the IDS received June 6, 2002, see entire document, particularly the right column of page 218, and also see lines 21-21 of page 13 of Valenta et al., WO 99/16467). As such a trimer of Bet v 1 does not show a diminution in specific IgE binding, and the specification does not appear to provide guidance or a working example concerning how to make a trimer of Bet v 1 that comprises this recited functional property. It should be noted that the specification does demonstrate that the trimer, when administered to experimental animal, did not elicit a significant IgE response that was directed to Bet v 1 (see particularly example 2 beginning on page 9 of the specification). The specification defines allergenic activity as the capacity to induce an IgE antibody response upon administration of a derivative to a test animal (see particularly page 4), and as such the Bet v 1 trimer has the functional property of reduced allergenic activity but does not

have the recited property of a diminished capacity to bind preexisting allergen specific IgE as compared to the wildtype allergen.

As discussed above, the Bet v 1 trimer does not comprise all of the recited functional properties, but the polypeptides consisting of amino acids 1-73 or 74-159 of Bet v 1 do comprise these activities as is evidenced by Vrtala et al. since they failed to bind IgE antibodies and induced blocking antibodies following their administration to a subject (J. Immunol., 2000, 165:6653-6659, see entire document, particularly the abstract).

However, there currently is no art recognized method to distinguish allergic from non-allergic molecules (such derivatives comprising fragments and oligomers of allergens that do not bind IgE) on an a priori structural basis (Blumenthal et al. in Allergens and Allergen Immunotherapy, 3rd edition, 2004, pages 37-50, see entire document, particularly the last sentence of the third complete paragraph of page 39). If the identity of the IgE binding epitopes in an allergen are precisely known, it is not predictable as to which amino acid positions within an epitope need to be altered by site directed mutagenesis such that IgE binding is abrogated (Burks et al., Eur. J. Biochem., 1997, 245:334-339, see entire document, particularly the top right column of page 338). Even when a precise amino acid within in the epitope to be altered is identified, the choice of what that amino acid should be mutated to by site directed mutagenesis is not predictable since some substituted amino acids reduce IgE binding while others have no effect or unexpectedly increase IgE binding (Nishiyama et al., US Patent 6,187,311, see entire document, particularly lines 4-30 of column 3, and Reese et al., J. Immunol., 2005, 175:8354-8364, see entire document, particularly the paragraph that spans pages 8357 and 8358, Table I and Figure 2). The specification does not appear to teach what changes are to be made naturally occurring allergens to make derivatives that satisfy the recited functional criteria, and the teachings of the art indicate that the structure of the material obtained as an immunotherapeutic agent at the conclusion of the screening protocol cannot be predicted. Given the above, it appears that a skilled artisan would need to rely on trial and error to identify derivatives suitable for use in the recited method, and since the claims are broad in that except for claims 46, 51, and 52 the

naturally occurring antigen is a member of a genus of allergens encompassing a very large number of members (see particularly chapter 11 of Lockey et al.) an undue amount of research would be required to practice the full breadth of applicant's claimed method.

Therefore, given that the claim recites the administration of agents derived from grass pollen allergens to treat all IgE-mediated disorders of any antigen specificity rather than those disorders that are specifically mediated by grass pollen specific IgE, the fact that an ongoing immune response, such as an IgE mediated disorder, cannot be effectively prevented since it has already occurred, the fact that applicant's example comprising a Bet v 1 trimer does not have all of the recited functional properties, and the difficulty of making the breath of claimed derivatives given the teachings of the specification and the art recognized difficulty in correlating the structural and functional properties of allergen derivatives, a skilled artisan would be unable to practice the full breadth of applicant's claimed invention without conducting an undue amount of additional research.

9. Claims 33, 34, 37-41, and 43-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed a method of treating or preventing IgE-mediated allergic disorders by repeatedly administering an agent to a patient, wherein the agent is a derivative of a naturally occurring allergen that has been selected via a screening protocol to identify derivatives that induce a blocking antibody response and that exhibit decreased allergen specific IgE binding as compared to the wildtype allergen. In support of the genus of administered agents that are allergen derivatives, applicant has provided three examples concerning the birch pollen allergen Bet v 1, namely a trimer of Bet v 1, the polypeptide consisting of amino acids 1-73 of Bet V 1 or the polypeptide

consisting of amino acids 74-159 of Bet v 1. This disclosure does not support the claimed genus for the reasons set forth below.

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

As discussed at length in paragraph 8 of this office action, the disclosed trimer of Bet v 1 does not comprise all of the recited functional properties, and as such it is not part of the recited genus of allergen derivatives. The two fragments of Bet v 1 do comprise all of the functional properties, but the independent claim is not limited to these particular fragments, or even to the birch pollen allergen Bet v 1. The recited genus of grass pollen allergens is very large and structurally diverse (see particularly chapter 11 of Lockey et al.), and applicant has defined derivatives in the paragraph spanning pages 2 and 3 of the specification to be fragments, oligomers, and chemically modified forms of naturally occurring allergens as well as molecules obtained by site directed mutagenesis of an allergen protein. The structure of these derivatives is not taught, and while functional properties are recited, the specification does not teach how these functional properties are correlated with structure. Further, the art teaches that correlations between structure and IgE binding (or the lack of IgE binding) cannot be predicted on an a priori structural basis (Blumenthal et al. in Allergens and Allergen Immunotherapy, 3rd edition, 2004, pages 37-50, see entire document, particularly the last sentence of the third complete paragraph of page 39). As such, the disclosure of the polypeptides consisting of amino acids 1-73 and consisting of amino acids 74-159 of Bet v 1 do not comprise a representative number of species to support the recited

genus of grass pollen allergen derivatives, and thus the recited genus lacks written description.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 33, 34, 37-40, 43-49, and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Vrtala et al. (J. Immunol., December 1, 2000, 165:6653-6659, see entire document).

Vrtala et al. teach a method of treating allergy by administering derivatives of Bet v 1 that induce the production of IgE-blocking antibodies and that are not bound by IgE antibodies that are specific for wildtype Bet v 1 (see entire document, particularly the abstract). The derivatives of Bet v 1 were repeatedly administered to mice and rabbits at intervals of greater than 14 days. Mice were immunized four times, each dose comprising 5 μg of the derivatives adsorbed onto complete Freund's adjuvant (CFA), while rabbits were immunized three times, with each dose comprising 200 μg adsorbed onto CFA (see particularly the section *Immunization of mice and rabbits and measurements of mouse IgG subclass responses* in the right column of page 6654). The instant claims do not recite that the intended patient population consists of humans, and the specification teaches in the middle of page 2 that the disclosed methods of treatment are applicable to both humans and animals. As such, CFA is a pharmaceutically acceptable adsorbate for animals such as mice and rabbits.

Therefore, the prior art anticipates the claimed invention.

12. Claims 33, 34, 37, and 46-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Valenta et al. (WO 99/16467 A1, see entire document) as evidenced by Vrtala et al. (J. Immunol., December 1, 2000, 165:6653-6659, see entire document).

Valenta et al. teach a method of treating allergy by repeatedly administering derivatives of Bet v 1 (see entire document, particularly the abstract and the paragraph spanning pages 5 and 6). The Bet v 1 derivatives comprise the polypeptides consisting of amino acids 1-73 of Bet v 1 and amino acids 74-159 of Bet v 1 (see particularly lines 9-20 of page 4 and pages 15-19). These polypeptides are taught as being combined with the pharmaceutically acceptable adsorbate and adjuvant aluminum hydroxide prior to *in vivo* administration (see particularly lines 2-9 of page 6). These polypeptides do not bind IgE isolated from known birch pollen allergenic patients, and thus they comprise reduced IgE binding as compared to wildtype Bet v 1 allergen (see particularly the paragraph spanning pages 17 and 18). Valenta et al. did not demonstrate that these polypeptides, when administered to a subject, induce a blocking antibody response. However, it is inherent that such a response to the polypeptides administered by Valenta et al. occurs as evidenced by Vrtala et al., who teach that administration of the same polypeptides as taught by Valenta et al. induce a blocking antibody response (see entire document, particularly the abstract, discussion, and Tables II and III).

Therefore, the prior art anticipates the instant invention.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 33, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vrtala et al. (J. Immunol., December 1, 2000, 165:6653-6659, see entire document) in view of Hem et al. (chapter 9 of Vaccine Design: The Subunit and Adjuvant Approach, 1995, pages 249-76, see entire document).

The teachings of Vrtala et al. have been discussed above. While Vrtala et al. teach that their allergen derivatives are to be used in methods of human administration (see entire document, particularly the abstract and discussion sections), these teachings differ from the instant claimed invention in that they do not teach the use of aluminum hydroxide as part of the administered composition.

Hem et al. teach that aluminum hydroxide is a widely used adjuvant that offers the important advantage of being the only adjuvant licensed by the food and Drug Administration for administration to human patients (see entire document, particularly the introduction).

Therefore, it would have been obvious at the time the invention was made to substitute aluminum hydroxide for the CFA used in the methods of administration taught by Vrtala et al. Motivation to make this substitution comes from the teachings of Vrtala et al. that their allergen derivative compositions are to be administered to humans and the teachings of Hem et al. that the only adjuvant that can be administered to human patients is aluminum hydroxide.

15. Claims 33, 38, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vrtala et al. (J. Immunol., December 1, 2000, 165:6653-6659, see entire document).

The teachings of Vrtala et al. have been discussed above. These teachings differ from the instant claimed method in that while Vrtala et al. teach repeated

administration of allergen derivatives wherein the period between administrations is at least 14 days, Vrtala et al. do not teach that the time interval between the third and fourth administrations is longer than the time interval between the first three administrations. However, it would have been obvious to a person of ordinary skill in the art at the time the invention was made modify the interval between administrations. As person of ordinary skill in the art at the time the invention was made would have been motivated modify the time intervals to optimize the treatment method, and determining the optimal intervals of administration of the allergen derivative is well within the purview of one of ordinary skill in the art at the time the invention was made. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). See MPEP § 2144.05 part II A.

16. No claims are allowable.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
June 5, 2006

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600